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EXAMINER	
BARTON, JEFFREY THOMAS	
ART UNIT	**PAPER NUMBER**
1753	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/743,698	GASCOYNE ET AL.	
	Examiner	Art Unit	
	Jeffrey T. Barton	1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 29 April 2005.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-56 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-56 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. The amendment filed on 29 April 2005 does not place the application in condition for allowance.

Status of Objections and Rejections Pending Since the Office Action of 27 October 2004

2. The objection to claim 12 is withdrawn due to Applicant's amendment.

3. The rejection of claims 1, 13, and 49-51 under 35 U.S.C. §102(b) as anticipated by Becker et al (WO 01/14870) is withdrawn due to Applicant's amendment.

4. All other rejections from the previous office action are maintained.

Claim Objections

5. Claim 29 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. As amended, claim 16 requires the use of a swept frequency signal in combination with a fixed frequency signal.

Claim Rejections - 35 USC § 103

6. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

7. Claims 1-6, 13, 44, 45, and 49-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Becker et al. (WO 01/14870)

Addressing method claims 1-6 and 13:

Relevant to claim 1, Becker et al disclose a method comprising: subjecting particles to a dielectrophoretic force by simultaneously applying two different signals to two different sets of electrodes (Figure 2D; Page 49, lines 10-21); using swept frequency signals and fixed frequency signals to create dielectrophoretic forces (Page 44, lines 13-22; Page 45, lines 3-15; Page 39, lines 13-26); segregating the particles into two or more zones of a surface (Page 25, lines 3-27; Page 29. lines 10-11); and attaching the particles to the surface. (Page 29, lines 10-11)

Relevant to claims 2-6, Becker et al disclose variation of electrode width and spacing that would result in varying field intensity along the length of the device (e.g. Page 11, lines 10-17), application of plural simultaneous electric fields of fixed or swept frequency (Page 45, lines 3-8; Page 7, lines 3-23), transitioning between zones of different electrical signals and electrode or channel geometry (Page 29, lines 7-10), and flexibility in operation and optimization of AC signal characteristics (Page 13, lines 10-23)

Relevant to claim 13, Becker et al disclose their method comprising flow DEP-FFF. (Summary section, especially Page 13, lines 20-23)

Becker et al do not explicitly disclose methods comprising the simultaneous application of a swept frequency signal to a first set of electrodes and a fixed frequency signal to a second set of electrodes (Claim 1); wherein the swept frequency signal falling from maximum to minimum intensity along a length of a surface, and the fixed frequency signal falling from maximum to minimum intensity in the opposite direction (Claim 2); linear or non-linear intensity variation (Claims 3 and 4); intensity controlled by electrode bus width (Claim 5); or non-zero minimum intensities of either signal. (Claim 6)

Regarding claim 1, it would have been obvious to one having ordinary skill in the art to modify the method of Becker et al by specifically applying swept and fixed frequency signals simultaneously to the two different sets of electrodes, because Becker et al teach the simultaneous application of signals having different frequency, amplitude and waveforms to the two sets of electrodes (Page 49, lines 17-21), and also teach the advantages of both swept (Page 45, lines 9-15) and fixed (Page 44, lines 2-12) frequency signals in causing dielectrophoretic forces needed for their field flow fractionation methods. Given the disclosure of Page 49, lines 17-21, the selection of any types of waveforms discussed by Becker et al (e.g. swept and fixed frequency)

would have been obvious to one having ordinary skill in the art, in order to optimize the separation of a given sample mixture.

Regarding claim 2, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Becker et al to provide a swept-frequency signal falling in intensity along a length of the chamber as a fixed-frequency signal rises in intensity along the same length, because Becker et al teach all device configurations needed to provide such a pattern, and it would provide a smooth transition between the zones of different separation parameters Becker et al suggest. (Page 29, lines 7-10)

Regarding claims 3 and 4, it would also have been obvious to provide linear or non-linear variation in intensity, because a linear variation would be the simplest pattern to apply, but the non-linear variation could provide greater or lesser periods of combined field influence on the particles, as dictated by the needs of the given separation.

Regarding claim 5, it would also have been obvious to vary signal intensity by varying electrode bus thickness, because it would be straightforward to prepare a suitable lithographic mask, and it is known that resistance and electric field strength are directly influenced by the cross section of the conductor. One having ordinary skill in the art would have recognized this as a straightforward, effective way varying signal intensity.

Regarding claim 6, it would also have been obvious to use non-zero intensity minima in cases where the continued influence of both fields is desirable for a particular separation.

Addressing apparatus claims 44, 45, and 49-51:

Relevant to claim 44, Becker et al disclose an apparatus comprising: a surface and electrodes near the surface (e.g. Figure 2D; Page 49, lines 10-14), multiple signal generators for providing swept or fixed frequency signals (Page 13, lines 11-13; Page 49, lines 17-21; Page 45, lines 3-8), electrodes of variable width and spacing that would result in varying field intensity along the length of the device (e.g. Page 11, lines 10-17), application of plural simultaneous electric fields of fixed or swept frequency (Page 45, lines 3-8; page 49, lines 10-21), transitioning between zones of different electrical signals and electrode or channel geometry (Page 29, lines 7-10), and flexibility in operation and optimization of AC signal characteristics (Page 13, lines 10-23); wherein the device can apply the signals to provide a dielectrophoretic force for particle separation. (Page 45, lines 3-8)

Relevant to claim 45, Becker et al disclose integral generators. (Page 13, lines 11-13)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify to apparatus of Becker et al to configure the signal generators to apply a swept-frequency signal falling in intensity along a length of the chamber and a fixed-frequency signal rises in intensity along the same length, because Becker et al teach all device configurations needed to provide such a pattern, and it would provide a smooth transition between the zones of different separation parameters Becker et al suggest. (Page 29, lines 7-10)

Relevant to claim 49, Becker et al disclose an apparatus comprising: a dielectrophoretic field flow fractionator that applies a dielectrophoretic force through the simultaneous application of two different signals to two sets of electrodes to separate particles (e.g. cells) into two or more zones (Figure 2D; Page 49, lines 10-21); and a dielectrophoretic collector coupled to the fractionator that attaches the particles to the surface. (Page 29, lines 4-11) The term "smear" can be applied to such attachment of cells to a surface. Becker et al also disclose using swept frequency signals and fixed frequency signals to create dielectrophoretic forces (Page 44, lines 13-22; Page 45, lines 3-15; Page 39, lines 13-26)

Relevant to claim 50, Becker et al disclose the smear comprising a pap smear. (Page 28, lines 11-15)

Relevant to claim 51, Becker et al disclose the fractionator and collector forming an integral unit. (Page 28, line 22 - Page 29, line 11)

It would have been obvious to one having ordinary skill in the art by modifying the device of Becker et al by specifically configuring it to apply swept and fixed frequency signals simultaneously to the two different sets of electrodes, because Becker et al teach the simultaneous application of signals having different frequency, amplitude and waveforms to the two sets of electrodes (Page 49, lines 17-21), and also teach the advantages of both swept (Page 45, lines 9-15) and fixed (Page 44, lines 2-12) frequency signals in causing dielectrophoretic forces needed for their field flow fractionation methods. Given the disclosure of Page 49, lines 17-21, the selection of

any types of waveforms discussed by Becker et al (e.g. swept and fixed frequency) would have been obvious to one having ordinary skill in the art, in order to optimize the separation of a given sample mixture.

In the rejections of apparatus claims, undue weight is not given to recitations of intended use of the apparatus. (e.g. "where the fixed frequency signal and the swept frequency signal are applied simultaneously" or descriptions of the form of the signals that are intended to be applied) A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

8. Claims 7-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Becker et al (WO 01/14870) in view of Seul et al.

Becker et al disclose a method as described above in addressing claim 1. They also disclose the possibility of including non-conducting elements to modify the flow profile for improved particle discrimination, (Page 29, lines 1-6) separation of particles using a flow, a cross-flow, and a dielectrophoretic force that opposes a force associated with the cross-flow. (Page 56, line 10 - Page 57, line 14; Page 58, lines 5-13)

Relevant to claim 10, Becker et al disclose dielectrophoretic force caused by electrodes near a dielectric substrate having openings. (Figure 13; both substrates have openings)

Relevant to claim 11, Becker et al disclose dielectrophoretic force caused by current passing through an opening in a dielectric barrier. (Figure 13; current must pass through either the substrate or the spacer, both are dielectric)

Becker et al do not explicitly disclose this method as "filtering", although its function is similar.

Seul et al disclose a method using a dielectrophoretic device with filtering elements within the chamber, the method also using flow and crossflow in opposition to dielectrophoretic forces. (Figure 9a; Column 19, line 45 - Column 20, line 15)

Relevant to claim 8, Seul et al illustrate their method involving a substantially perpendicular crossflow. (Figure 9a)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Becker et al by performing it within a chamber that comprises filtering elements, as taught by Seul et al, because it would provide an additional mode of separation to assist in discriminating between similar particles.

Regarding claim 8, it would also have been obvious to provide a substantially perpendicular crossflow, as taught by Seul et al, because it would provide the greatest effect for a given crossflow. Regarding claim 9, having simultaneous adjustable flow

and crossflow is functionally equivalent to having non-perpendicular crossflow, as identical flow profiles within the chamber are attainable.

9. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Becker et al (WO 01/14870) in view of Giddings et al.

Becker et al disclose a method as described above in addressing claim 1. Additionally, they disclose the possibility of including non-conducting elements to modify the flow profile for improved particle discrimination (Page 29, lines 1-6) and sedimentation of separated particles (Page 14, lines 5-9)

Becker et al do not explicitly disclose a method using a physical barrier to confine particles in a particular zone.

Giddings et al disclose a dielectrophoretic method using collection ports defined at valleys in a corrugated surface (i.e. periodic barriers) to confine particles in discrete zones. (Abstract, Figure 1)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Becker et al by performing it within a chamber that comprises collection ports positioned at valleys defined by periodic physical barriers, as taught by Giddings et al, because it would provide a relatively simple method of separating particles based on size.

10. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Becker et al (WO 01/14870) in view of Arnold.

Becker et al disclose a method as described above in addressing claim 1.

Becker et al do not explicitly disclose a method in which growth of the particles (i.e. cells) on the surface is promoted.

Arnold discloses a dielectrophoretic separation method for cells in which growth of the cells within the chamber is promoted by the composition of the liquid medium. (Column 4, lines 35-37) Some growth would occur at the chamber surfaces.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Becker et al by promoting growth of the separated cells, as taught by Arnold, because it would provide enhanced ability to detect dilute cell species, enhancing process sensitivity.

11. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Becker et al (WO 01/14870) in view of Cheng et al.

Becker et al disclose a method as described above in addressing claim 1. They also disclose using a computer to control the applied voltage. (Page 45, lines 16-21)

Becker et al do not explicitly disclose a method in which the applied signals are automatically adjusted as a function of the conductivity of the suspending medium.

Cheng et al disclose general automation of microfluidic chip-based biological analyses, including dielectrophoretic manipulation of cells and voltage control. (Abstract, Paragraphs 0004 and 0057-0059)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Becker et al by automating voltage control,

as taught by Cheng et al, because it would reduce the manual labor required for analysis. Furthermore, it would also be obvious to control the voltage as a function of medium conductivity because it is a critical parameter linked to resistive heating of the device, which could potentially degrade the sample.

12. Claims 16-18, 20-25, 28-34, 42, and 52-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Becker et al (WO 01/14870) in view of the website of Tripath Imaging, Inc. (March 5, 2002).

Addressing claims 16-18, 20-25, 28-34, and 42:

Relevant to claim 16, Becker et al disclose a method comprising: subjecting particles of a sample to dielectrophoretic force through the simultaneous application of two different signals to two sets of electrodes to segregate the particles into two or more zones of a surface (Figure 2D; Page 49, lines 10-21; Page 45, lines 3-8; Page 39, lines 13-26; and Page 29, lines 10-11); and attaching the particles to the surface, defining a segregated smear. (Page 29, lines 10-11) Becker et al also suggest the use of their device and method to perform pap smear analyses (Page 28, lines 11-15), and they disclose using swept frequency signals and fixed frequency signals to create dielectrophoretic forces (Page 44, lines 13-22; Page 45, lines 3-15; Page 39, lines 13-26)

Relevant to claim 18, Becker et al disclose attaching particles to the surface by dielectrophoretic force. (Page 29, lines 10-11)

Relevant to claim 20, Becker et al disclose attaching particles to the surface by allowing particles to settle. (Page 14, lines 5-9)

Relevant to claim 21, Becker et al disclose the particles comprising cells. (Page 3, line 24 - Page 4, line 2)

Relevant to claim 22, Becker et al disclose the smear comprising a pap smear. (Page 28, lines 11-15)

Relevant to claims 23-25, Becker et al disclose the dielectrophoretic force arising from simultaneous application of programmed voltage signals of different frequencies (Page 45, lines 3-8); application of frequencies exhibiting one or more DEF-FFF and trapping phases (Page 7, line 3 - Page 11, line 17; Page 13, lines 10-23, Page 29, lines 10-11); and generation of the force by electrodes coupled to the surface. (Figure 13)

Relevant to claim 28, Becker et al disclose the separation of particles into distinct bands. (Page 3, line 14 - Page 4, line 2)

Relevant to claim 29, Becker et al disclose using a swept frequency signal in combination with a fixed frequency signal. (Page 45, lines 3-8; Figure 6F; Page 39, lines 13-26)

Relevant to claim 30, Becker et al disclose variation of electrode width and spacing that would result in varying field intensity along the length of the device (e.g. Page 11, lines 10-17), application of plural simultaneous electric fields of fixed or swept frequency (Page 45, lines 3-8; Page 7, lines 3-23), transitioning between zones of different electrical signals and electrode or channel geometry (Page 29, lines 7-10), and

flexibility in operation and optimization of AC signal characteristics (Page 13, lines 10-23)

Relevant to claim 42, Becker et al disclose separation of particles by DEP-FFF. (Summary section, especially Page 13, lines 20-23)

Relevant to claim 16, Becker et al do not explicitly disclose the simultaneous application of a swept frequency signal to a first set of electrodes and a fixed frequency signal to a second set of electrodes, nor do they disclose fixing or staining the segregated smear.

Relevant to claims 30-34, Becker et al also do not explicitly disclose methods comprising the swept frequency signal falling from maximum to minimum intensity along a length of a surface, and the fixed frequency signal falling from maximum to minimum intensity in the opposite direction; linear or non-linear intensity variation; intensity controlled by electrode bus width, or non-zero minimum intensities of either signal.

Relevant to claim 16, the website of Tripath Imaging, Inc. (March 5, 2002) disclosed kits and reagents, including fixatives and stains for performing pap smear analyses. (Surepath™ test pack, Prepstain™ slide processor)

Regarding claim 16, it would have been obvious to one having ordinary skill in the art to modify the method of Becker et al by specifically applying swept and fixed frequency signals simultaneously to the two different sets of electrodes, because

Becker et al teach the simultaneous application of signals having different frequency, amplitude and waveforms to the two sets of electrodes (Page 49, lines 17-21), and also teach the advantages of both swept (Page 45, lines 9-15) and fixed (Page 44, lines 2-12) frequency signals in causing dielectrophoretic forces needed for their field flow fractionation methods. Given the disclosure of Page 49, lines 17-21, the selection of any types of waveforms discussed by Becker et al (e.g. swept and fixed frequency) would have been obvious to one having ordinary skill in the art, in order to optimize the separation of a given sample mixture.

It would also have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Becker et al including steps of fixing and staining the pap smear sample, as taught by the Tripath website, because they are standard steps in pap smear analysis.

Relevant to claim 30, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify to method of Becker et al to provide a swept-frequency signal falling in intensity along a length of the chamber as a fixed-frequency signal rises in intensity along the same length, because Becker et al teach all device configurations needed to provide such a pattern, and it would provide a smooth transition between the zones of different separation parameters Becker et al suggest. (Page 29, lines 7-10)

Relevant to claims 31 and 32, it would also have been obvious to provide linear or non-linear variation in intensity, because a linear variation would be the simplest pattern to apply, but the non-linear variation could provide greater or lesser periods of

combined field influence on the particles, as dictated by the needs of the given separation.

Relevant to claim 33, it would also have been obvious to vary signal intensity by varying electrode bus thickness, because it would be straightforward to prepare a suitable lithographic mask, and it is known that resistance and electric field strength are directly influenced by the cross section of the conductor.

Relevant to claim 34, it would also have been obvious to use non-zero intensity minima in cases where the continued influence of both fields is desirable for a particular separation.

Addressing claims 52-54:

Becker et al disclose an apparatus described in addressing claim 49 in paragraph 7 above.

Becker et al do not explicitly disclose a machine reader configured to evaluate particles (Claim 52); a fixing stage and staining stage coupled to the collector (Claim 53); or fixing and staining stages coupled to the collector to form an integral unit. (Claim 54)

The website of Tripath Imaging, Inc. (March 5, 2002) disclosed an automated diagnostic system allowing integrated sample preparation, staining, and screening, that would correspond to these claimed embodiments. (Focalpoint™ slide profiler)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the apparatus of Becker et al by coupling the collector to

an automated, integrated workstation that performs fixation, staining, and screening, as taught by the Tripath website, because the website teaches that its use decreases operator labor and increases the reliability of analyses.

13. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Becker et al (WO 01/14870) and the website of Tripath Imaging, Inc. (March 5, 2002) as applied to claim 16 above, and further in view of Coster et al.

Becker et al (WO 01/14870) and the Tripath website disclose a combined method as described above in addressing claim 16.

Neither Becker et al nor the Tripath website disclose using an adhesive to bind cells to the surface.

Coster et al disclose a dielectrophoretic separation method involving binding of cells to the surface of their device using an adhesive.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combined method of Becker et al and the Tripath website by using an adhesive to hold cells to the surface, as taught by Coster et al, because it would help prevent sample loss without requiring electrical power.

14. Claims 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Becker et al (WO 01/14870) and the website of Tripath Imaging, Inc. (March 5, 2002) as applied to claims 16 and 25 above and further in view of Becker et al. (US 5,858,192)

Becker et al (WO 01/14870) and the Tripath website disclose a combined method as described above in addressing claims 16 and 25. Becker et al also disclose flexibility in electrode shape within their devices and methods. (Page 6, lines 7-22; Page 29, lines 6-10)

Neither Becker et al (WO 01/14870) nor the Tripath website explicitly disclose a method in which the electrodes are configured in a spiral (Claim 26), or wherein the zones are concentric circular zones. (Claim 27)

Becker et al (US 5,858,192) disclose a dielectrophoretic separation device comprising spiral electrodes, and methods for its use. (Abstract, Figure 2B) They also disclose the zones wherein the particles attach to the surface being concentric circular zones. (Figures 5 and 6)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combined method of Becker et al (WO 01/14870) and the Tripath website by using spiral-shaped electrodes that cause particles to be disposed in concentric zones, as taught by Becker et al (US 5,858,192), because Becker et al (WO 01/14870) disclosed flexibility in chamber and electrode geometry, and it would facilitate concentration and collection of the cells directed to the center of the device.

15. Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Becker et al (WO 01/14870) and the website of Tripath Imaging, Inc. (March 5, 2002) as applied to claim 29 above and further in view of Cheng et al.

Becker et al and the Tripath website disclose a combined method as described above in addressing claim 29. Becker et al also disclose using a computer to control the applied voltage. (Page 45, lines 16-21)

Neither Becker et al nor the Tripath website explicitly disclose a method in which the applied signals that cause dielectrophoresis are automatically adjusted as a function of the conductivity of the suspending medium.

Cheng et al disclose general automation of microfluidic chip-based biological analyses, including dielectrophoretic manipulation of cells and voltage control. (Abstract, Paragraphs 0004 and 0057-0059)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combined method of Becker et al and the Tripath website by automating voltage control, as taught by Cheng et al, because it would reduce the manual labor required for analysis. Furthermore, it would also be obvious to control the voltage as a function of medium conductivity because it is a critical parameter linked to resistive heating of the device, which could potentially degrade the sample.

16. Claims 36-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Becker et al (WO 01/14870) and the website of Tripath Imaging, Inc. (March 5, 2002) as applied to claim 16 above and further in view of Seul et al.

Becker et al and the Tripath website disclose a combined method as described above in addressing claim 16. Becker et al also disclose the possibility of including non-

conducting elements to modify the flow profile for improved particle discrimination, (Page 29, lines 1-6) separation of particles using a flow, a cross-flow, and a dielectrophoretic force that opposes a force associated with the cross-flow. (Page 56, line 10 - Page 57, line 14; Page 58, lines 5-13)

Relevant to claim 39, Becker et al disclose dielectrophoretic force caused by electrodes near a dielectric substrate having openings. (Figure 13; both substrates have openings)

Relevant to claim 40, Becker et al disclose dielectrophoretic force caused by current passing through an opening in a dielectric barrier. (Figure 13; current must pass through either the substrate or the spacer, both are dielectric)

Becker et al do not explicitly disclose this method as "filtering", although its function is similar. The Tripath website discloses no such filtering methods.

Seul et al disclose a method using a dielectrophoretic device with filtering elements within the chamber, the method also using flow and crossflow in opposition to dielectrophoretic forces. (Figure 9a; Column 19, line 45 - Column 20, line 15)

Relevant to claim 37, Seul et al illustrate their method involving a substantially perpendicular crossflow. (Figure 9a)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combined method of Becker et al and the Tripath website by performing it within a chamber that comprises filtering elements, as taught by Seul et al, because it would provide an additional mode of separation to assist in discriminating between similar particles.

Regarding claim 37, it would also have been obvious to provide a substantially perpendicular crossflow, as taught by Seul et al, because it would provide the greatest effect for a given crossflow. Regarding claim 38, having simultaneous adjustable flow and crossflow is functionally equivalent to having non-perpendicular crossflow, as identical flow profiles within the chamber are attainable.

17. Claim 41 is rejected under 35 U.S.C. 103(a) as being unpatentable over Becker et al (WO 01/14870), the website of Tripath Imaging, Inc. (March 5, 2002), and Seul et al as applied to claim 36 above and further in view of Giddings et al.

Becker et al, the website of Tripath Imaging, Inc., and Seul et al disclose a method as described above in addressing claim 36. Additionally, Becker et al disclose the possibility of including non-conducting elements to modify the flow profile for improved particle discrimination (Page 29, lines 1-6) and sedimentation of separated particles (Page 14, lines 5-9)

Becker et al do not explicitly disclose a method using a physical barrier to confine particles in a particular zone.

Giddings et al disclose a dielectrophoretic method using collection ports defined at valleys in a corrugated surface (i.e. periodic barriers) to confine particles in discrete zones. (Abstract, Figure 1)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Becker et al by performing it within a chamber that comprises collection ports positioned at valleys defined by periodic

physical barriers, as taught by Giddings et al, because it would provide a relatively simple method of separating particles based on size.

18. Claim 43 is rejected under 35 U.S.C. 103(a) as being unpatentable over Becker et al (WO 01/14870) and the website of Tripath Imaging, Inc. (March 5, 2002) as applied to claim 16 above and further in view of Arnold.

Becker et al and the Tripath website disclose a combined method as described above in addressing claim 16.

Neither Becker et al nor the Tripath website explicitly disclose a method in which growth of the particles (i.e. cells) on the surface is promoted.

Arnold discloses a dielectrophoretic separation method for cells in which growth of the cells within the chamber is promoted by the composition of the liquid medium. (Column 4, lines 35-37) Some growth would occur at the chamber surfaces.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Becker et al by promoting growth of the separated cells, as taught by Arnold, because it would provide enhanced ability to detect dilute cell species, enhancing process sensitivity.

19. Claims 46 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Becker et al (WO 01/14870) in view of Seul et al.

Becker et al disclose an apparatus as described above in addressing claim 44. They also disclose the possibility of including non-conducting elements to modify the

flow profile for improved particle discrimination, (Page 29, lines 1-6) separation of particles using a flow, a cross-flow, and a dielectrophoretic force that opposes a force associated with the cross-flow. (Page 56, line 10 - Page 57, line 14; Page 58, lines 5-13)

Becker et al do not explicitly disclose a filter coupled to the surface.

Seul et al disclose a dielectrophoretic device with filtering elements within the chamber, coupled to a surface of the device, wherein particles are subjected to flow and crossflow in opposition to dielectrophoretic forces. (Figure 9a; Column 19, line 45 - Column 20, line 15) These filtering elements are disclosed as oxide grown from the surface that comprises the electrodes. (Column 19, lines 45-54)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Becker et al by providing the chamber with filtering elements, as taught by Seul et al, because it would provide an additional mode of separation to assist in discriminating between similar particles.

20. Claim 48 is rejected under 35 U.S.C. 103(a) as being unpatentable over Becker et al (WO 01/14870) in view of Giddings et al.

Becker et al disclose an apparatus as described above in addressing claim 44. Additionally, they disclose the possibility of including non-conducting elements to modify the flow profile for improved particle discrimination (Page 29, lines 1-6) and sedimentation of separated particles (Page 14, lines 5-9)

Becker et al do not explicitly disclose a method using a physical barrier to confine particles in a particular zone.

Giddings et al disclose a dielectrophoretic device comprising collection ports defined at valleys in a corrugated surface (i.e. periodic barriers) to confine particles in discrete zones. (Abstract, Figure 1)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Becker et al by providing the chamber with collection ports positioned at valleys defined by periodic physical barriers, as taught by Giddings et al, because it would provide a relatively simple method of separating particles based on size.

21. Claims 55 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over the website of Tripath Imaging, Inc. (March 5, 2002) in view of Becker et al. (WO 01/14870)

The website of Tripath Imaging, Inc. (March 5, 2002) disclosed kits comprising fixing agents and pap smear staining agents. (Prepstain™ slide processor)

The website of Tripath Imaging, Inc. did not disclose a surface comprising electrode sets for applying any dielectrophoretic force to particles.

Becker et al disclose a device comprising surfaces comprising arrays of electrodes adapted to subject particles to dielectrophoretic force to segregate the particles into two or more zones. (Figure 2D) They also disclose using this device to subject particles to a dielectrophoretic force by simultaneously applying two different

signals to two different sets of electrodes (Figure 2D; Page 49, lines 10-21); and using swept frequency signals and fixed frequency signals to create dielectrophoretic forces. (Page 44, lines 13-22; Page 45, lines 3-15; Page 39, lines 13-26)

It would have been obvious to modify the kits of Tripath Imaging, Inc. to include surfaces (i.e. slides) comprising electrodes configured for operation in the device of Becker et al because it would provide a supply of the needed consumable/disposable items for numerous pap smear analyses, as contemplated by Becker et al. (Page 28, lines 11-15)

In rejecting these kit claims, undue weight is not given to recitations of intended use of elements of the kits. (i.e. "simultaneously applying a swept frequency signal . . . and a fixed frequency signal") A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

Response to Arguments

22. Applicants' arguments filed 29 April 2005 have been fully considered but they are not persuasive. In the arguments presented in the paragraph bridging pages 9 and 10 or the amendment, Applicants describe one embodiment of the system of Becker et al in detail, concluding that this disclosure "does not amount to disclosure or suggestion of subjecting particles of a sample to a dielectrophoretic force by simultaneously applying

a swept frequency signal to a first set of electrodes and a fixed frequency signal to a second set of electrodes, as required by claim 1."

The Examiner agrees that Becker et al do not explicitly disclose the new limitations added in the amendment of 29 April 2005, and thus the rejection under 35 U.S.C. §102(b) has been withdrawn. However, the disclosure of Becker et al is broader than described by Applicants in the amendment, and a rejection under 35 U.S.C. §103(a) is considered to be appropriate, based on the citations given in the rejections above. As presented above, the use of signals with differing frequency and waveform applied to two different sets of electrodes was taught by Becker et al (Figure 2D; Page 49, lines 10-21), as were the advantages of using either fixed or swept frequency signals. (Page 44, lines 2-12; Page 45, lines 9-15) Since there are a limited number of signal types taught by Becker et al (i.e. fixed or varying frequency, amplitude, and waveform), the choice of these two types of signals would have been obvious to one having ordinary skill in the art, given the disclosure of Page 49, lines 17-21.

The remainder of Applicants' arguments (Pages 10-17) is directed to the patentability of all claims based on the patentability of the independent claims that incorporated variations of the same limitation that is addressed above. Applicants point out that the secondary references cited do not teach the new limitations, and the Examiner agrees. However, no specific arguments were addressed to the reasoning presented in the previous rejections under 35 U.S.C. §103(a), and these rejections are therefore maintained.

Conclusion

23. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Jeffrey Barton, whose telephone number is (571) 272-1307. The examiner can normally be reached Monday-Friday from 8:30 am – 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen, can be reached at (571) 272-1342. The fax number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

JTB
June 22, 2005

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